Bern – November 22nd, 2017

(13:00-13:45)

Symposium for Infectious Diseases

How to stay ahead in the race against resistant pathogens

Emerging clinical needs not covered with the current automation

Prof. Andrea Endimiani, MD, PhD

Institute for Infectious Diseases (IFIK)

University of Bern, Switzerland

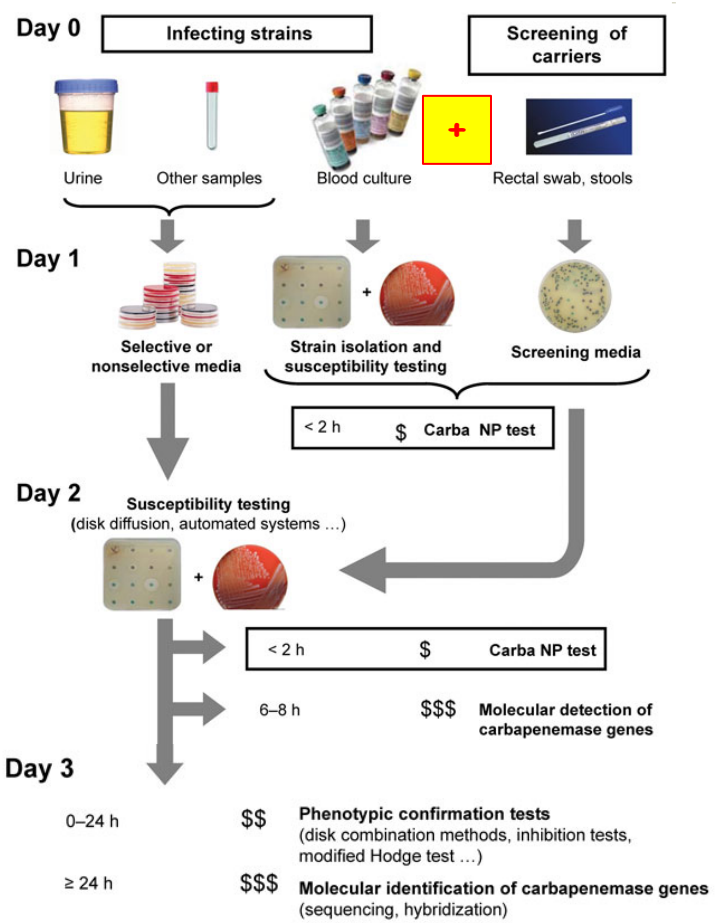
TREATMENT SETTING

- **Rapid species identification and antibiogram**
  - for serious infections (e.g., BSIs)
  - for patients at risk (e.g., traveled/admitted from ≠ countries, in ICU)
  - enable effective antibiotic stewardship interventions
- **Rapid detection of key resistance mechanisms or genes**
  - ESBLs and carbapenemases
  - affecting other key antibiotics (e.g., polymyxins)
- **Rapid MIC values for key antibiotics**
  - Cefepime, carbapenems, polymyxins …….

HOSPITAL HYGIENE SETTING

- **Rapid screening to identify patients colonized with MDR bacteria**
  - ➢ for isolation (prevention of outbreaks, save costs)
- **Rapid identification of clonal MDR strains**
  - ➢ identifying sources, tracking dynamics, intervention
- **Microbiological lab data and algorithms ***

Standard culture approach



Even more days to get the final report including resistance mechanism(s)/gene(s)

Empirical treatment

Isolation

Directed treatment

Outcome

Septic shock

Inappropriate antibiotic use within the first 6 hours is associated with a 5-fold higher mortality risk

[Kumar A *et al.*, Chest, 2009]

BSIs

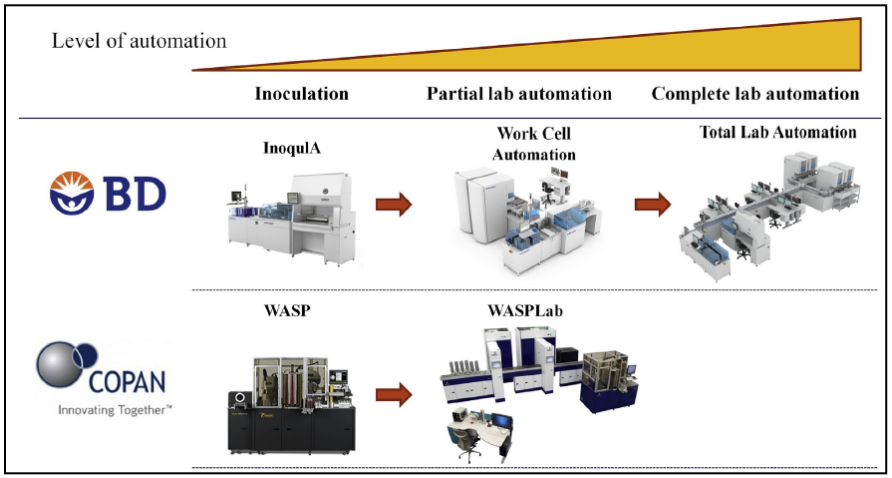
Mean decrease in survival of 7.6% for each hour after the onset of BSI until initiation of effective antibiotics

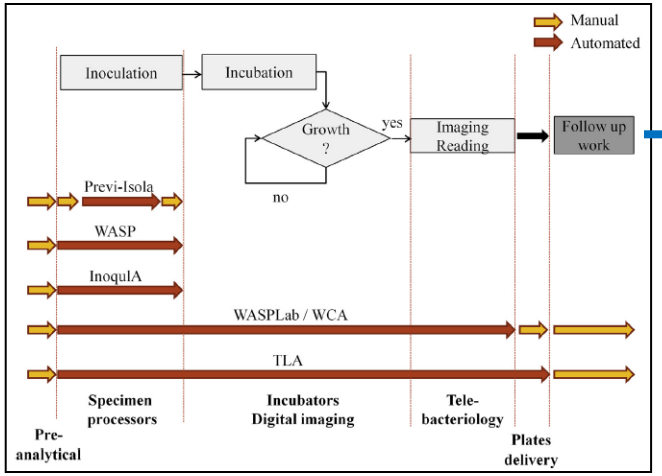
[Kumar A *et al.*, Crit Care Med, 2006]

MDR Gram-neg BSI

It costs 30.000 $ more (11 vs. 6 days of hospitalization)

[Schwaber MJ et al., JAC, 2007]





ID/AST Still standard

Advantages
Activity/productivity (increase processing of diagnostic samples).

- Improvement of laboratory workflow (dashboards).
- Management reports.
- Cost savings.

Quality and reproducibility.

- Inoculation: Improved yield of isolated colonies.
- Incubation: Improved bacterial growth.

Reduced time to results (ID and AST).

- Decrease hospitalization time, decrease risks of nosocomial infections, treatment improvements.
- Cost savings.

Traceability (barcodes).

- Decrease errors (e.g. sample, media plates, broth switching).

Security.

- Decrease plate transportation.

Labor saving.

- Decrease fastidious and repetitive tasks (e.g. inoculation, plates incubation).
- Release expert staff for added value tasks (e.g. pre- and postanalytic phase, reading, interpretation, troubleshooting, R&D, microscopy).
- Reduce overtime payments.

diagnostic laboratory. Thus, the real benefits of lab automation remain to be demonstrated in objective, comparative and prospective clinical studies performed by independent laboratories and published in peer-reviewed journals. Several

A. Croxatto[1], G. Prod'hom[1], F. Faverjon[2], Y. Rochais[3] and G. Greub[1]
Clinical Microbiology and Infection, Volume 22 Number 3, March 2016

Total Laboratory Automation and MALDI-TOF Improve Turnaround Times in the Clinical Microbiology Laboratory: a Retrospective Analysis

Theparee T et al., JCM Nov 8, 2017

Bruker MALDI-TOF MS (Oct, 2013) - BD Kiestra TLA (Dec, 2014)

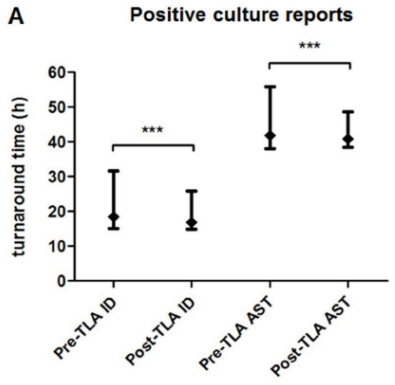
STUDY AIM: TAT for +/- urine cultures before and after implementation

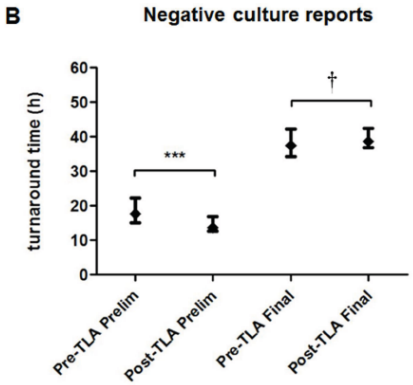
Comparison I: Impact of Kiestra TLA

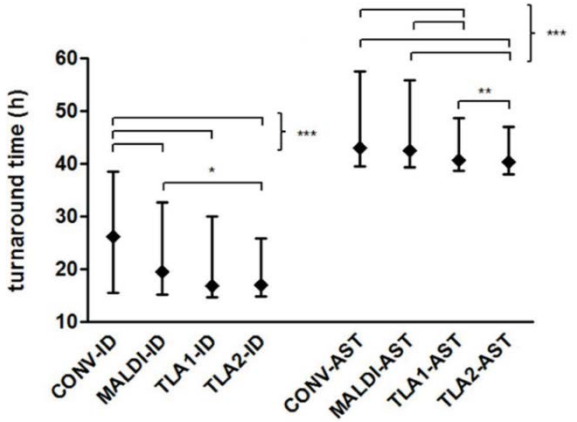
	Time to ID or preliminary negative		Time to AST or final negative	
	Pre-TLA	Post-TLA	Pre-TLA	Post-TLA
Negative cultures	17.73 h	13.62 h	37.38 h	38.62 h
(N=42,259)	(14.97-22.25)	(12.60-16.80)***	(34.35-42.17) †	(36.85-42.53) †
Positive cultures	18.53 h	16.92 h	41.80 h	40.85 h
(N=17,251)	(15.00-31.62)	(14.95-25.87)***	(38.08-55.78)	(38.53-48.68)***

Comparison II: Impact of MALDI and/or Kiestra TLA

	CONV	MALDI	TLA1	TLA2
Overall				
Time to ID	21.33 h	18.02 h	16.45 h	16.79 h
	(14.96-36.79)	(14.70-30.70)	(14.67-24.28)	(14.83-23.55)
Time to AST	42.74 h	42.33 h	40.70 h	40.33 h
	(39.55-57.43)	(39.30-55.38)	(38.65-47.73)	(38.07-47.08)



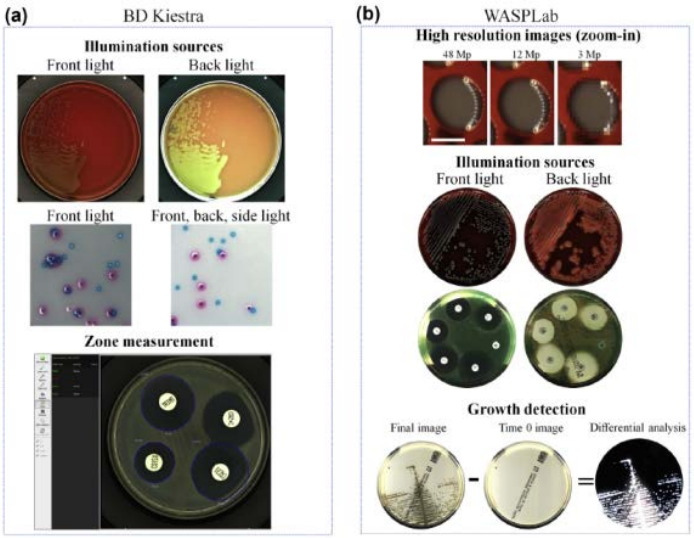




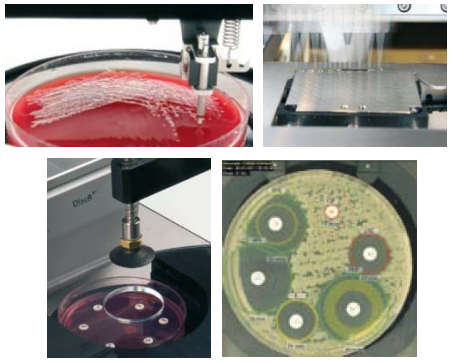
Future developments on lab automation

MALDI-TOF MS

SMART IMCUBATORS



Automated colony picking for ID and AST (e.g., MaldiTofA and Colibri)



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Automated disk diffusion AST preparation

Automated inhibition zone measurements

Expert systems for dynamic AST interpretation

Automated direct screening for resistance of Gram-negative blood cultures using the BD Kiestra WorkCell

C. S. Heather[1] · M. Maley[1]

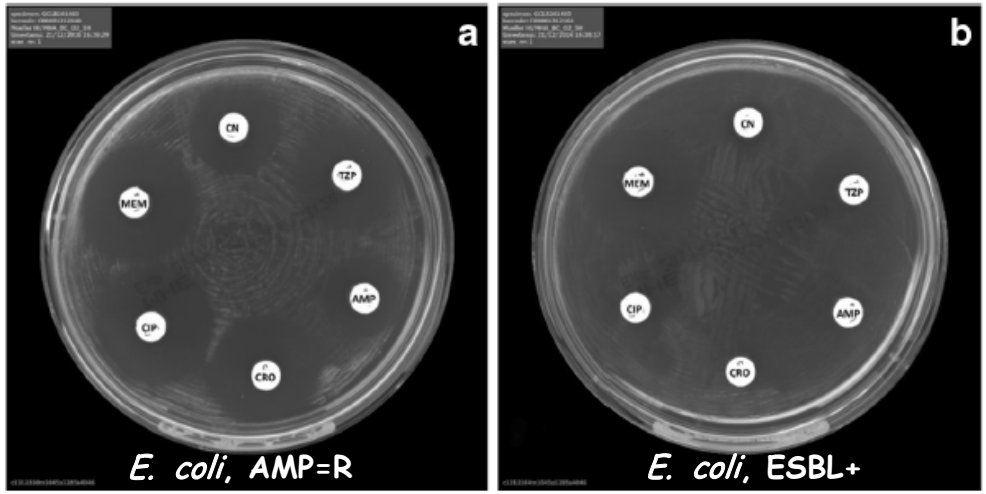
Eur J Clin Microbiol Infect Dis
02 October 2017

BACTEC 187 +BCs for G- → 2 drops in Copan ESwab → Kiestra InoqulA MH plates → Pre-loaded disk stamp → Kiestra InoqulA MH plates → **Kiestra ReadA incubators**

15 min

BD ReadA Browser software
(Inhib. zone marked manually)

Digital image of automated direct screening for resistance (5 hrs)



AST *Enterobacteriaceae* at 5 hrs *vs.* VITEK2

	Cut-off	Sensitivity (95% CI)	Specificity (95% CI)	Non-susceptible isolates (%)
Ampicillin	13 mm	98.3 (93.9–99.8)	98.2 (90.3–99.9)	67.6
Ceftriaxone	19 mm	100 (92.6–100)	99.2 (95.5–99.9)	28.2
Piperacillin–tazobactam	20 mm	87.0 (66.4–97.2)	84.7 (77.8–90.2)	13.8
Meropenem	21 mm	93.8 (69.8–99.8)	94.8 (90.0–97.7)	9.4
Ciprofloxacin	17 mm	96.6 (82.2–99.9)	95.7 (91.0–98.4)	17.1
Gentamicin	14 mm	97.4 (86.2–99.9)	100 (97.1–100)	23.5

82.8% were evaluable at 4 hrs

AST *P. aeruginosa* at 8 hrs *vs.* VITEK2

Antibiotic (zone size cut-off)	Sensitivity (95% CI)	Specificity (95% CI)	Non-susceptible isolates (%)
Ampicillin (13 mm)	100 (73.5–100)	N/A[a]	100
Ceftriaxone (19 mm)	91.7 (61.5–99.8)	N/A[a]	100
Piperacillin–tazobactam (20 mm)	100 (2.5–100)	100 (71.5–100)	7.7
Meropenem (21 mm)	100 (15.8–100)	80 (44.4–97.5)	7.7
Ciprofloxacin (17 mm)	100 (2.5–100)	100 (71.5–100)	7.7
Gentamicin (14 mm)	100 (2.5–100)	90.9 (58.7–99.8)	7.7

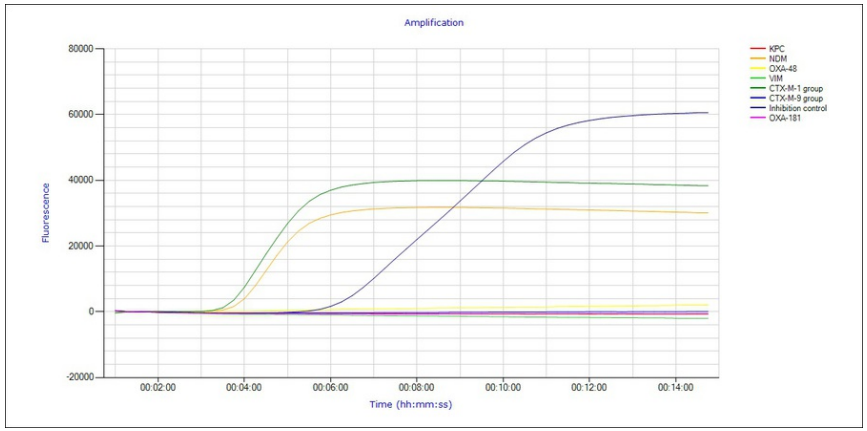
Ideal system

- Species identification (ID)
- AST (MIC) and interpretation (S, I, R)
- Genes and/or resistance mechanisms
- Kit and automated (easy to use)
- High sensitivity/specificity
- Clinical samples (or at least +BCs)
- Rapid
- Cost-effective

Amplex Eazyplex

Genie II platform

- Preparation (**5 min**)
- No DNA extraction/purification
- Run time (**<30 min**)



LAMP
Loop-mediated isothermal Amplification

Real-time fluorescent measurement

~55 Euro

eazyplex® MRSA

S. aureus
mecA
mecC
S. epidermidis

eazyplex® VRE

eazyplex® SuperBug mcr-1

eazyplex® SuperBug CRE

KPC,
NDM,
OXA-48
and OXA 181,
VIM, as well as
CTX-M-1 and
CTX-M-9 group

eazyplex® SuperBug complete

Version A	Version B
KPC	KPC
NDM	NDM
OXA-48	OXA-48
VIM	VIM
OXA-23 group	OXA-23 group
OXA-40 group	OXA-40 group
OXA-58 group	OXA-181

Evaluation of loop-mediated isothermal amplification for the rapid identification of bacteria and resistance determinants in positive blood cultures

Rödel J. *et al.*, Eur J Clin Microbiol Infect Dis; 2017

Germany, 2015
370 +BCs (of which 140 G+)
Test preparation from 25 µL of +BC: 5-10 min

Table 1 Analytes detected by the eazyplex® assays used in this study[a]

MRSA	GP	GN
S. aureus	*E. faecalis*	*E. coli*
S. epidermidis	*Enterococcus* spp.	*K. pneumoniae*
mecA	*S. pneumoniae*	Enterobacteriaceae
mecC	*Streptococcus* spp.	*Pseudomonas* spp.
	vanA	$bla_{\text{CTX-M-1}}$ group
	vanB	$bla_{\text{CTX-M-9}}$ group

eazyplex® MRSA

In-house LAMP assays (not available)

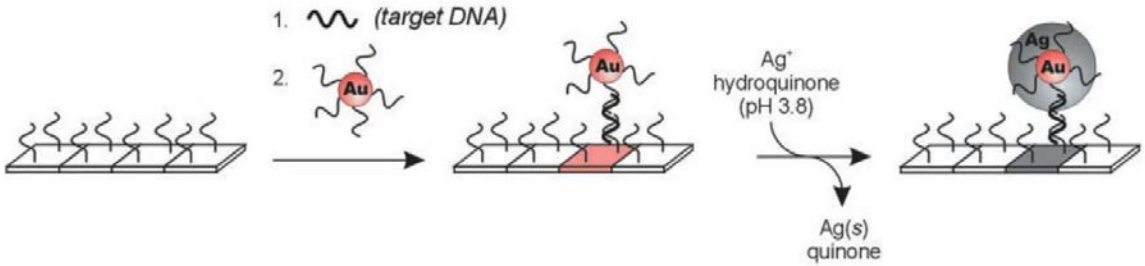
ID § Resistance	True-positive (*n*)	True-negative (*n*)	False-positive (*n*)	False-negative (*n*)	No. positive/no. tested (%) (95% CI[a])	
					Sensitivity	Specificity
MRSA						
S. aureus	31	106	2	0	100 (88.8–100)	98.2 (93.5–99.8)
MRSA[d]	6	25	0	0	100 (54.1–100)	100 (86.3–100)
S. epidermidis	72	60	1	6	92.3 (84–97.1)	98.4 (91.2–100)
mecA (CoNS)	73	30	0	3	96 (88.9–99.2)	100 (88.4–100)
GP						
E. faecalis	12	58	1	0	100 (73.5–100)	98.3 (90.9–100)
Enterococcus spp.	41	27	2	1	97.6 (87.4–99.9)	93.1 (77.2–99.1)
VRE[e]	3	39	0	0	100 (29.2–100)	100 (91–100)
S. pneumoniae	2	69	0	0	100 (15.8–100)	100 (94.8–100)
Streptococcus spp.	20	50	0	1	95.2 (76.2–99.9)	100 (92.9–100)
GN						
E. coli	97	58	2	0	100 (96.3–100)	96.7 (88.5–99.6)
E. coli CTX-M[f]	17	80	0	0	100 (89.5–100)	100 (95.5–100)
E. coli ESBL[g]	17	78	0	2	89.5 (66.9–98.7)	100 (95.3–100)
K. pneumoniae	11	143	2	1	91.7 (61.5–99.8)	98.6 (95.1–99.8)
K. pneumoniae ESBL[h]	4	7	0	0	100 (39.8–100)	100 (59–100)
Enterobacteriaceae	134	12	11	2	98.5 (94.8–99.8)	52.2 (30.6–73.2)
Pseudomonas spp.	9	148	0	0	100 (66.4–100)	100 (97.5–100)

Time to results	Threshold time [min; mean values (SD)]	
	True-positive	False-positive
MRSA		
S. aureus	7 (1.5)	17
mecA (*S. aureus*)	11.5 (4)	–
S. epidermidis	11.75 (2.75)	18.75
mecA (CoNS)	9.75 (2.5)	–
IC	7.5 (1)	–
GP		
E. faecalis	6.75 (1)	17.5
Enterococcus spp.	10 (4)	17.5
vanA	7 (1)	–
vanB	–	–
S. pneumoniae	7	–
Streptococcus spp.	13.5 (3.25)	–
IC	9.5 (0.75)	–
GN		
E. coli	7.25 (1.75)	15
K. pneumoniae	13.75 (2.5)	10.75
$bla_{\text{CTX-M-1}}$ group[a]	8.5 (4)	–
$bla_{\text{CTX-M-9}}$ group[b]	6.25 (1)	–
Enterobacteriaceae	6.25 (1.75)	15.75 (2.5)
Pseudomonas spp.	8.25 (1.5)	–
IC	9 (1.75)	–

From +BC ~30 min

Verigene, Nanosphere

- Load cartridge, consumables, and sample (**5 min**)
- Automated sample preparation and processing
- Place slide from cartridge in reader (**2.5 hrs**)



Microarray approach by using Au-nanoprobe as reporter and silver reduction to enhance signal

Gram-negatives cartridge

Species	Genus	Resistance
Escherichia coli	*Acinetobacter* spp.	CTX-M (ESBL)
Klebsiella pneumoniae	*Citrobacter* spp.	IMP (carbapenemase)
Klebsiella oxytoca	*Enterobacter* spp.	KPC (carbapenemase)
Pseudomonas aeruginosa	*Proteus* spp.	NDM (carbapenemase)
Serratia marcescens		OXA (carbapenemase)
		VIM (carbapenemase)

Gram-positives cartridge

Species	Genus	Resistance
Staphylococcus aureus	*Staphylococcus* spp.	*mecA* (methicillin)
Staphylococcus epidermidis	*Streptococcus* spp.	*vanA* (vancomycin)
Staphylococcus lugdunensis	*Micrococcus* spp.	*vanB* (vancomycin)
Streptococcus anginosus Group	*Listeria* spp.	
Streptococcus agalactiae		
Streptococcus pneumoniae		
Streptococcus pyogenes		
Enterococcus faecalis		
Enterococcus faecium		

~50 Euro

Performance Evaluation of the Verigene Gram-Positive and Gram-Negative Blood Culture Test for Direct Identification of Bacteria and Their Resistance Determinants from Positive Blood Cultures in Hong Kong

Gilman K.H. Siu *et al.*, Plos One, Oct 2015

Multicenter study (4 hospitals), 2014

364 BCs (114 Gram-pos; 250 Gram-neg)

ID for Gram-positives (agreement 89.6%)

Organisms	No. (%) of isolates Total	Correctly identified	Not detected	Misidentified	No Call	Sensitivity (%)	Specificity (%)
Staphylococcus spp.	73 (60.3)	69 (94.5)	-	-	4	100	100
S. aureus	48 (39.7)	47 (97.9)	-	-	1	100	100
S. epidermidis	4 (3.3)	4 (100)	-	-	-	100	100
Streptococcus spp.	27 (22.3)	25 (92.6)	-	-	2	100	98.9
S. pyogenes	2 (1.7)	2 (100)	-	-	-	100	100
S. agalactiae	3 (2.5)	3 (100)	-	-	-	100	100
S. anginosus gr.	1 (0.8)	1 (100)	-	-	-	100	100
S. pneumoniae	7 (5.8)	7 (100)	-	-	-	100	99.1
E. faecalis	7 (5.8)	4 (57.1)	2 (28.6)	-	1	66.7	100
E. faecium	5 (4.1)	2 (40)	2 (40)	-	1	50	100
Listeria	1 (0.8)	1 (100)	-	-	-	100	100

ID for Gram-negatives (agreement 90.5%)

Organisms	No. (%) of isolates Total	Correctly identified	Not detected	Misidentified	No Call	Sensitivity (%)	Specificity (%)
E.coli	165 (59.1)	158 (95.8)	6 (3.6)	1[c]	-	95.8	100
K. pneumoniae	52 (18.6)	36 (69.2)	14 (27)[d]	2[e]	-	69.2[d]	100
P. aeruginosa	17 (6.1)	13 (76.5)	3 (17.6)	-	1	81.3	100
Proteus spp.	10 (3.6)	9 (90)	-	-	1	100	100
Enterobacter spp.	10 (3.6)	8 (80)	-	-	2	100	99.3
Acinetobacter spp.	4 (1.4)	4 (100)	-	-	-	100	100
K. oxytoca	3 (1.1)	-	3 (100)	-	-	0	99.3
Citrobacter spp.	1 (0.4)	1 (100)	-	-	-	100	100

K. variicola 80%

A. hydrophila, M. morganii, Salmonella spp., A. faecalis, B. pseudomallei, H. influenzae, R. planticola, P. putida, S. maltophilia **not detectable with the system** (n=16; 5.5%)

MDR organisms

Drug resistant Organisms	No. of isolates Total	Correctly Detected	Not Detected	No Call	Sensitivity	Specificity (%)
Gram Positive						
MRSA	27	26	0	1	100	100
MRSE	4	4	0	0	100	100
VRE	1	1	0	0	100	100
Gram Negative						
Cefotaxime resistant *Enterobacteriaceae* (including ESBL producers)	61	38	22	1	63.3	100
ESBL producing *Enterobacteriaceae*	46	38	7	1	84.4	100
MDR *Acinetobacter*	3	3	0	0	100	100
Carbapenem-resistant *Psuedomonas*	2	0	2	0	0	100
Total	**98**	**72**	**24**	**2**	**75.0**	**100**

Time to Results (40-99 hrs faster than routine)

Organisms	No. of Isolates[b]	Average Time to identification by Culture-Based Method (h)	Average Time to Result by Verigene Test (h)	Δ Time to Result[a] Average (h)	Range (h)	*p*-value
Staphylococcus spp.	23	63.76	2.35	61.41	22.65–494.65	*p*<0.001
MSSA	7	49	2.35	46.65	22.65–79.65	*p* = 0.012
MRSA	10	93.45	2.35	91.1	23.65–494.65	*p*<0.001
CNS	8	57.19	2.35	54.84	29.65–97.65	*p*<0.001
Streptococcus spp.	13	63.86	2.35	61.51	22.65–128.15	*p*<0.001
S. pneumoniae	3	42.83	2.35	40.48	22.65–56.65	p = 0.017
β-haemolytic Strept.	4	71.62	2.35	69.27	33.65–128.15	*p*<0.001
Viridians Group	6	55.08	2.35	52.73	25.65–83.65	*p*<0.001
Enterococcus spp.	2	78.5	2.35	76.15	53.15–99.15	*p*<0.001
VSE	1	55.5	2.35	53.15	n/a	n/a
VRE	1	101.5	2.35	99.15	n/a	n/a
Enterobacteriaceae	79	45.98	1.88	44.1	18.12–104.12	*P*<0.001
P. aeruginosa	7	52.51	1.88	50.63	28.62–94.62	*p*<0.001
Acinetobacter spp.	1	76	1.88	74.12	n/a	n/a

Clinical Impact of Laboratory Implementation of Verigene BC-GN Microarray-Based Assay for Detection of Gram-Negative Bacteria in Positive Blood Cultures

Walker T. *et al.*, J Clin Microbiol; 54:7, 2016

Los Angeles
May 2013 - Nov 2013
Dec 2014 – May 2015

6-month period before Verigene (n=98) *vs.* 6-month period after Verigene (n=97)

Inpatient stay = 1,400 USD/day
ICU stay = 2,800 USD/day
Test cost (all incl.) = 99 USD

Clinical outcome

	Pre-BC-GN	Post-BC-GN	*P* value
Mean time from initial Gram stain to BC-GN identification, h	NA[a]	3.5	NA
Mean time from initial Gram stain to organism identification, h	37.9	10.9	<0.001[b]
Mean time from initial Gram stain to effective therapy, h			
All cases	10.2	6.5	0.12[b]
Cases on suboptimal empirical therapy	30.3	19.1	0.12[b]
No. of cases in which therapy was de-escalated	33	37	0.66[c]
Mean time from initial Gram stain to de-escalation, h	40.9	34.1	0.14[b]
Recurrence of bacteremia, no. (%)	8 (8.2)	3 (3.1)	0.21[c]
Mean total length of stay in hospital, days	15.2	18.0	0.52[b]
Mean length of hospital stay after positive culture, days	9.7	9.4	0.87[b]
Mean length of stay in ICU, days	16.2	12.0	0.03[b]
30-day mortality, no. (%)	19 (19.2)	8 (8.1)	0.04[c]
ESBL cases, no.	15	11	0.53[c]
Length of stay in hospital, days	12.0	13.5	0.59[b]
Mean time to effective therapy, h (no.)[d]	41.4 (9)	7.3 (9)	0.04[b]
30-day mortality, no. (%)	4 (26.7)	0 (0)	0.11[c]

Saved 11,661 USD/case

Factors associated to length of ICU stay

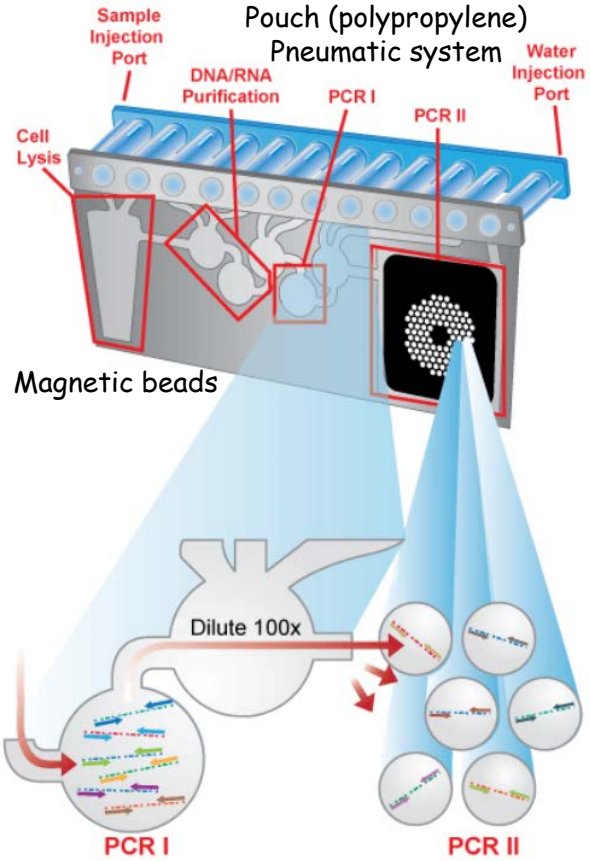
	Univariate analysis[b]			Multivariate analysis[b]		
Factor	HR	95% CI	*P* value	HR	95% CI	*P* value
Intervention	1.62	1.03–2.54	0.04	1.79	1.07–2.98	0.03
Preinfection length of stay	0.97	0.95–0.99	0.001	0.97	0.95–0.98	0.0001
Age	1.01	0.99–1.03	0.22	1.0	0.98–1.01	0.90
Sex (female)	0.64	0.40–1.03	0.06	0.69	0.41–1.15	0.15
Time to effective therapy	1.01	0.78–1.32	0.94	1.02	0.75–1.38	0.90
Disease severity (APACHE II)	1.00	0.97–1.02	0.74	0.97	0.93–1.0	0.06
Mortality	1.03	0.57–1.65	0.91	1.43	0.83–2.48	0.20

Multiv. log. regression for association with 30-d mortality

Factor	Odds ratio	95% CI	*P* value
Intervention	0.81	0.67–0.98	0.03
Length of stay, ICU	1.00	1.00–1.00	0.94
Age	1.01	1.00–1.01	0.11
Sex (female)	1.07	0.88–1.30	0.48
APACHE II	1.01	0.99–1.02	0.36

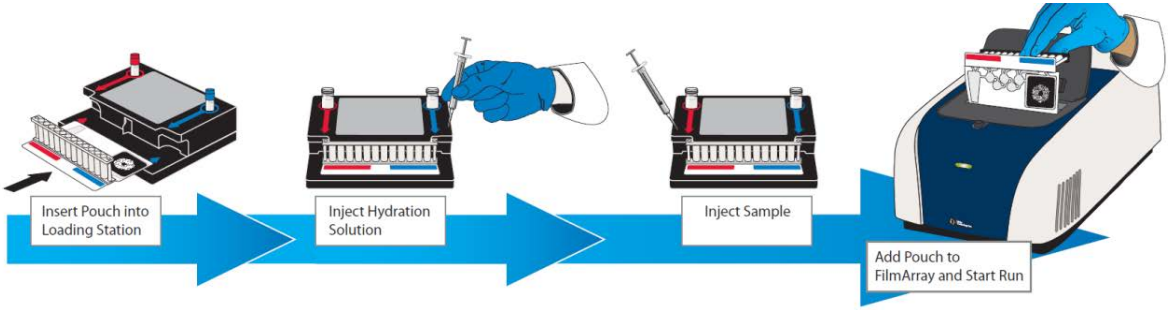
BioFire FilmArray

- Preparation of the pouch
- Add pouch to FilmArray station (overall, **2 min**)
- Run time of about **1 h**



Multiplex PCR
(RT-PCR for RNA target)

Multiplex real-time PCR
and Melting analysis



~100 Euro

FilmArray® BCID Panel targets:

Gram+ Bacteria	Gram– Bacteria
Enterococcus *Listeria monocytogenes* *Staphylococcus* *Staphylococcus aureus* *Streptococcus* *Streptococcus agalactiae* *Streptococcus pyogenes* *Streptococcus pneumoniae*	*Acinetobacter baumanniiHaemophilus influenzae* *Neisseria meningitidis* *Pseudomonas aeruginosa* *Enterobacteriaceae* *Enterobacter cloacae complex* *Escherichia coli* *Klebsiella oxytoca* *Klebsiella pneumoniae* *Proteus* *Serratia marcescens*
Yeast	**Antibiotic Resistance**
Candida albicans *Candida glabrata* *Candida krusei* *Candida parapsilosis* *Candida tropicalis*	mecA - methicillin resistance vanA/B - vancomycin resistance KPC - carbapenem resistance

Species ID

	Isolates detected[a]: BCID/comparator		No. of results: BCID/comparator					
	Clinical arm	Seeded arm	TP +/+	FP +/−	FN −/+	TN −/−	Sensitivity or PPA[b]: TP/(TP + FN) (%)	Specificity or NPA[b]: TN/(TN + FP) (%)
Gram-positive bacteria								
Enterococcus	102/101	29/29	127	4	3	2,073	127/130 (97.7)	2,073/2,077 (99.8)
L. monocytogenes	0/0	36/36	36	0	0	2,171	36/36 (100)	2,171/2,171 (100)
Staphylococcus	780/797	2/1	770	12	28	1,397	770/798 (96.5)	1,397/1,409 (99.1)
S. aureus	257/257	0/0	253	4	4	1,946	253/257 (98.4)	1,946/1,950 (99.8)
Streptococcus	140/141	63/62	198	5	5	1,999	198/203 (97.5)	1,999/2,004 (99.8)
S. agalactiae (group B)	18/18	18/18	36	0	0	2,171	36/36 (100)	2,171/2,171 (100)
S. pneumoniae	26/25	12/12	36	2	1	2,168	36/37 (97.3)	2,168/2,170 (99.9)
S. pyogenes (group A)	8/7	31/31	38	1	0	2,168	38/38 (100)	2,168/2,169 (99.9)
Total	1,331/1,346	191/189	1,494	28	41	16,093	1,494/1,535 (97.3)	16,093/16,121 (99.8)
Gram-negative bacteria								
A. baumannii	16/14	40/37	51	5	0	2,151	51/51 (100)	2,151/2,156 (99.8)
Enterobacteriaceae	307/310	187/188	490	4	8	1,705	490/498 (98.4)	1,705/1,709 (99.8)
E. cloacae complex	24/22	17/17	38	3	1	2,165	38/39 (97.4)	2,165/2,168 (99.9)
E. coli	149/148	6/5	150	5	3	2,049	150/153 (98.0)	2,049/2,054 (99.8)
K. oxytoca	6/6	54/58	59	1	5	2,142	59/64 (92.2)[c] 98%	2,142/2,143 (99.9)
K. pneumoniae	74/71	37/34	102	9	3	2,093	102/105 (97.1)	2,093/2,102 (99.6)
Proteus	22/22	17/17	39	0	0	2,168	39/39 (100)	2,168/2,168 (100)
S. marcescens	22/22	55/55	76	1	1	2,129	76/77 (98.7)	2,129/2,130 (99.9)
H. influenzae	8/8	35/35	43	0	0	2,164	43/43 (100)	2,164/2,164 (100)
N. meningitidis	1/1	35/35	36	0	0	2,171	36/36 (100)	2,171/2,171 (100)
P. aeruginosa	52/52	0/0	51	1	1	2,154	51/52 (98.1)	2,154/2,155 (99.9)
Total	681/676	483/481	1135	29	22	23,091	1,135/1,157 (98.1)	23,091/23,120 (99.9)

R. ornithinolytica

Evaluation of the FilmArray Blood Culture Identification Panel: Results of a Multicenter Controlled Trial

Salimnia H.. *et al.*, J Clin Microbiol; 54:3, 2016

8 centers in USA, 2012-2014

2,207 BC samples

- 1,568 clinical
- 639 seeded

MDR Organisms

Antimicrobial resistance gene(s)	Isolates detected: BCID/comparator Clinical arm	Seeded arm	No. of results: BCID/comparator TP +/+	FP +/−	FN −/+	TN −/−	Sensitivity or PPA[a]: TP/(TP + FN) (%)	Specificity or NPA[a]: TN/(TN + FP) (%)
mecA in association with:								
All *Staphylococcus* isolates detected[b]	491/494	2/2	488	5	8	281	488/496 (98.4)	281/286 (98.3)
Staphylococcus and *S. aureus* isolates detected	137/139	0/0	137	0	2	118	137/139 (98.6)	118/118 (100)
vanA/B in association with *Enterococcus* isolates detected	36/36	28/28	64	0	0	67	64/64 (100)[c]	67/67 (100)
bla_{KPC} in association with *Enterobacteriaceae* and/or *A. baumannii* and/or *P. aeruginosa* isolates detected	6/6[d]	33/33	39	0	0	558	39/39 (100)[e]	558/558 (100)

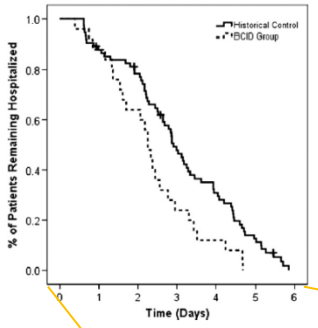
Clinical and economic impact of antimicrobial stewardship interventions with the FilmArray blood culture identification panel

Pardo J et al., DMID; 84, 2016

Gainesville, Florida

Intervention group (FilmArray)
(Aug 2013 – Jan 2014; n=84)
vs.
Historical control group
(Jan 2012 – Jun 2013; n=252)

55% CoNS



Time to discharge after CoNS-contaminated BCs

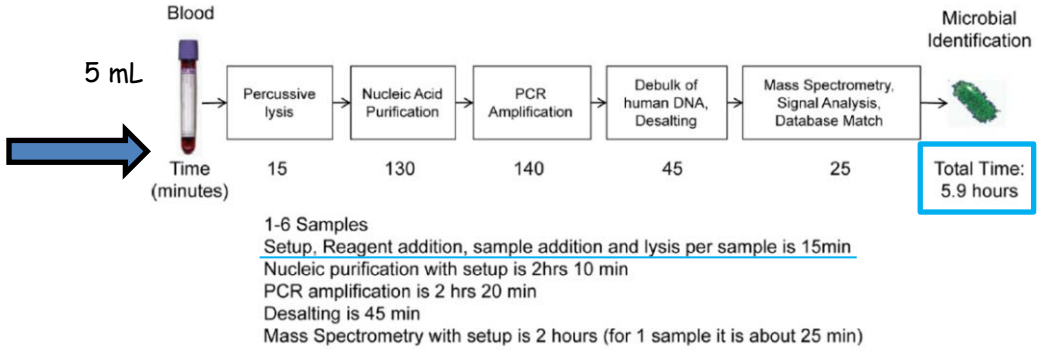
Variable	All Patients ($N = 336$)			Discharged Within 6 Days of CoNS Contamination ($N = 100$)		
	Control group ($N = 252$)	BCID group ($N = 84$)	P	Control group ($N = 75$)	BCID group ($N = 25$)	P
Median LOS (days [IQR])	7.9 (3.8–16.3)	7.4 (3–11.7)	0.178	2.9 (2.1–4.4)	2.3 (1.5–3.1)	0.008
Median ICU Days (IQR)	0 (0–5)	0 (0–1)	0.026	0 (0–0)	0 (0–0)	0.838
In-hospital mortality (No. [%])	37 (15)	5 (6)	0.036	4 (6)	0 (0)	0.239
Median Costs ($ [IQR])						
Total	15324 (5517–37305)	12241 (3080–21027)	0.030	3370 (1537–5190)	1645 (585–2952)	0.016
Pharmacy	2119 (598–5503)	1538 (366–3824)	0.073	429 (157–712)	214 (75–361)	0.010
Ward room	2806 (0–7427)	3972 (947–8041)	0.514	1852 (891–2778)	947 (0–1828)	0.025
ICU room	1222 (0–10218)	0 (0–3756)	0.008	0 (0–0)	0 (0–0)	0.659
Laboratory	708 (241–1804)	656 (254–1445)	0.692	160 (83–253)	204 (160–321)	0.020

129 USD for the test

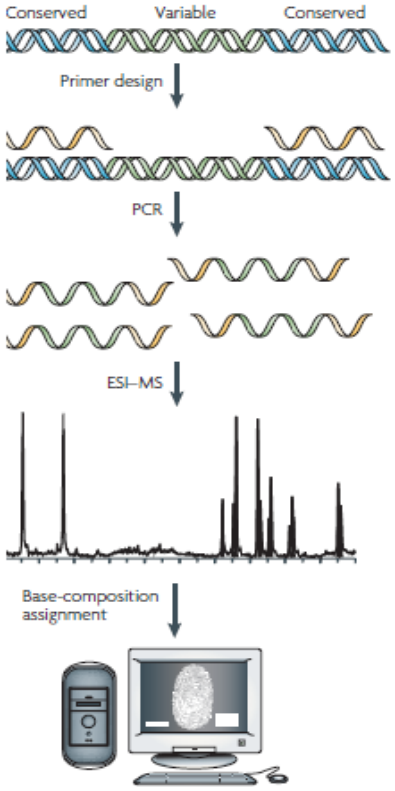
Unnecessary vancomycin use

Variable	MSSA (N = 32)			CoNS Contaminants (N = 184)		
	Control Group (N = 24)	BCID Group (N = 8)	P	Control Group (N = 138)	BCID Group (N = 46)	P
Vancomycin started (No. [%])	24 (100)	8 (100)	>0.99	100 (72)	32 (70)	0.705
1 dose only (No. [%])	0/24 (0)	4/8 (50)	0.002	12/100 (12)	7/32 (22)	0.133
Median duration (h [IQR])	66.0 (54.1–78.1)	14.0 (1–20)	<0.001	66.9 (37.6–135)	39.3 (14.7 –96.5)	0.100

Abbott IRIDICA PCR-ESI MS system



1-6 Samples
Setup, Reagent addition, sample addition and lysis per sample is 15min
Nucleic purification with setup is 2hrs 10 min
PCR amplification is 2 hrs 20 min
Desalting is 45 min
Mass Spectrometry with setup is 2 hours (for 1 sample it is about 25 min)



Ibis T5000, Abbott PLEX-ID

780 Bacteria and Candida, 4 Resistance Markers	Whole blood	IRIDICA BAC BSI Assay
	Sterile fluids and tissues	IRIDICA BAC SFT Assay
	BAL*, ETA**	IRIDICA BAC LRT Assay

KPC, VanA, VanB, mecA

~200-300 Euro

The IRIDICA BAC BSI Assay: Rapid, Sensitive and Culture-Independent Identification of Bacteria and *Candida* in Blood

Metzgar D. *et al.*, PlosOne; July 2016

Johns Hopkins Hospital; Baltimore, USA

285 whole blood samples (with SIRS)

Samples processed by Ibis Bioscience

Limit of detection (LOD) in blood: 16-32 CFU/mL

273 (95.7%) valid results

61 negative controls: all negative by IRIDICA

Organisms detected: IRIDICA, n=85; culture, n=45

11 of these 46 pathogens gave subsequent infection

Species ID

	Matched Positive	BAC BSI Assay + / Culture –	BAC BSI Assay –/ Culture +	Matched Negative[B]
Gram-positive (including Mycoplasma)	15	11[A(5)]	2	207
Gram-negative	13	21[A(4)]	3	207
Unidentified bacteria	0	1	0	207
Yeast	2	1	0	207
Potential Contaminants (details in Table 4)	2	12[A(2)]	3	207
Other reportable organisms excluding potential contaminants (n = 550)	0	0	0	207

32 out of 40 by culture (80% agreement)

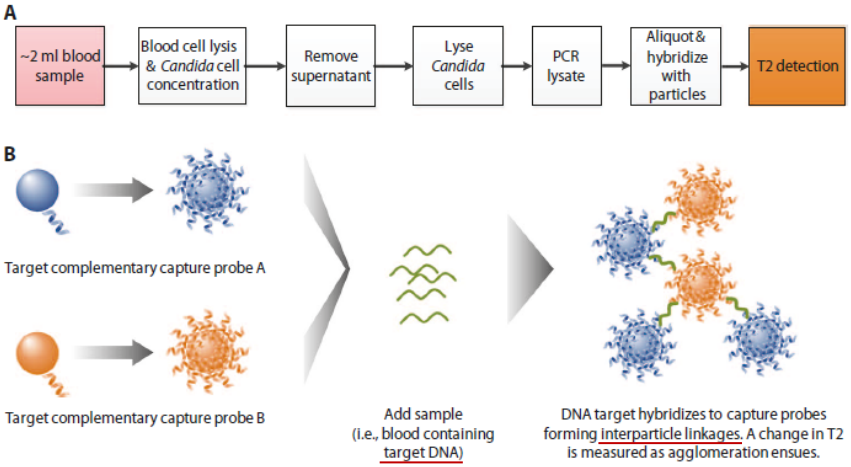
Antibiotic R markers

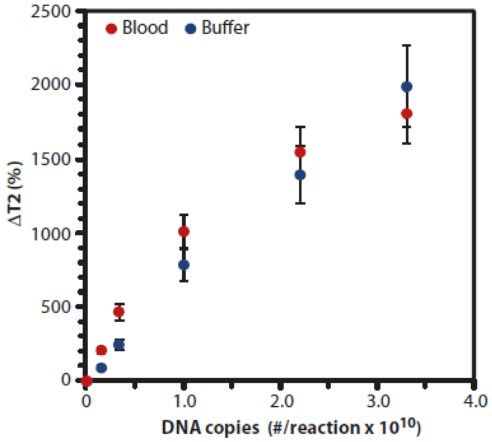
	Matched Positive	BAC BSI Assay + / Culture –	BAC BSI Assay –/ Culture +	Matched Negative
bla_{KPC} (carbapenem resistance[A])	0	0	0	0
vanA/vanB (vancomycin resistance[A])	0	0	0	4
mecA (methicillin resistance[A])	6	0	0	3

13/13

T2 Magnetic Resonance (T2MR)

- Sample transferred to T2Dx (1 min)
- **No extraction/purification**
- Time to results (**~3 hrs**)
- **Limit of detection: 1 CFU/mL**





T2Bacteria Kit

- Gram-negatives: *E. coli, K. pneumoniae, P. aeruginosa, A. baumannii*
- Gram-positives: *S. aureus, E. faecium*

Accelerate Pheno™ System (BC Kit)

Fully Automated

Entire process with 1 kit

2 min to load and start

Directly from +BC bottle

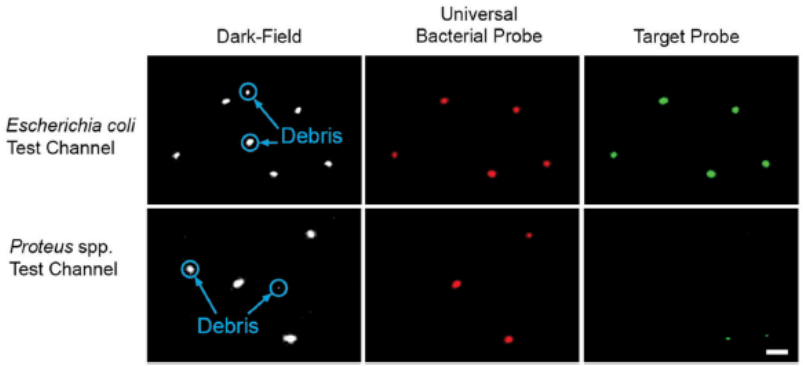
→

ID: <1.5 hrs

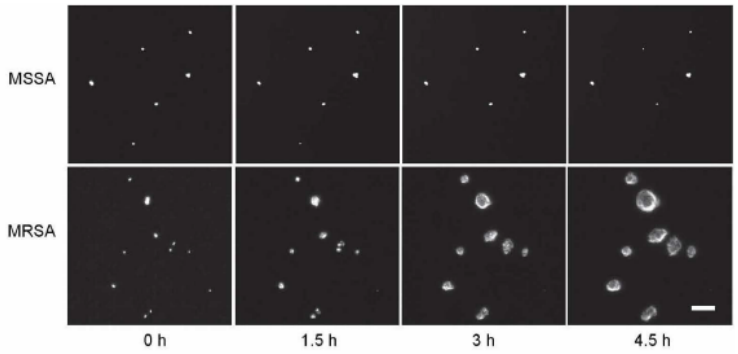
AST: <7 hrs

~120 Euro

ID: 16 FISH probes



AST: morphokinetic cell analysis



Gram-positive	Identification	Ampicilin	Ceftaroline	Erythromycin	Daptomycin	Linezolid	Vancomycin	MRSA (Cefoxitin)	MLSb (Erythromycin-Clindamycin)
S. aureus	•		•	•	•	•	•	•	
S. lugdunensis	•						•	•	•
CNS spp.	•				•		•	•	•
E. faecalis	•	•			•	•	•		
E. faecium	•	•			•	•	•		
Streptococcus spp.	•								

Gram-negative	Identification	Ampicillin-Sulbactam	Piperacillin-Tazobactam	Cefepime	Ceftazidime	Ceftriaxone	Ertapenem	Meropenem	Amikacin	Gentamicin	Tobramycin	Ciprofloxacin	Aztreonam
E. coli	•	•	•	•	•	•	•	•	•	•	•	•	•
Klebsiella spp.	•	•	•	•	•	•	•	•	•	•	•	•	•
Enterobacter spp.	•		•	•	•	•	•	•	•	•	•	•	•
Proteus spp.	•	•	•	•	•	•	•	•	•	•	•	•	•
Citrobacter spp.	•		•	•	•	•	•	•	•	•	•	•	•
S. marcescens	•		•	•	•	•	•	•	•	•	•	•	•
P. aeruginosa	•		•	•	•			•	•	•	•	•	
A. baumannii	•		•						•				

Evaluation of the Accelerate Pheno System for Fast Identification and Antimicrobial Susceptibility Testing from Positive Blood Cultures in Bloodstream Infections Caused by Gram-Negative Pathogens *Marschal M et al., JCM, July 2017*

April 2016 – Oct 2016: Southern Germany

115 BSIs due to Gram-negatives (10 poly)

Routine: BACTEC 9240, MALDI, Vitek2, Etest

ACC started on average 8 h after positive signal

Identification

Correct ID:

102/115 (88.7%)

Correct ID for covered species:

102/105 (97.1%)

e.g., B. fragilis, M. morganii, H. alvei not detected

Accelerate Pheno system AST

Antimicrobial agent	No. of AST results	No. (%) of category agreements S	R/I	Total	No. (%) of minor discrepancies	No. (%) of major discrepancies	No. (%) of very major discrepancies
SAM	66	31	32	63 (95.5)	0 (0)	3 (8.8)	0 (0)
TZP	91	78	6	84 (92.3)	0 (0)	7 (8.2)	0 (0)
FEP	90	73	6/1*	80 (88.9)	7 (7.8)	3 (3.6)	0 (0)
CRO	85	75	8	83 (97.6)	0 (0)	2 (2.6)	0 (0)
ETP	85	85	0	85 (100)	0 (0)	0 (0)	0 (0)
MEM	94	91	2	93 (98.9)	1 (1.1)	0 (0)	0 (0)
AMK	95	91	2	93 (97.9)	1 (1.1)	0 (0)	1 (33.3)
GEN	94	84	9	93 (98.9)	0 (0)	1 (1.2)	0 (0)
TOB	94	82	10	92 (97.9)	1 (1.1)	1 (1.2)	0 (0)
CIP	94	69	21	90 (95.7)	4 (4.3)	0 (0)	0 (0)
CST	88	85	0	85 (96.6)	0 (0)	3 (3.4)	0 (0)
Total	976	844	97	941 (96.4)	14 (1.4)	20 (2.3)	1 (1.0)

MIC (μg/ml)[c]

Isolate (n = 13)	Test[b]	SAM	TZP	FEP	CRO	ETP	MEM	AMK	GEN	TOB	CIP	CST	Comment
C. freundii (1)	ACC	–	128 (R)	≤1 (S)	≥8 (R)	0.25 (S)	≤0.25 (S)	≤4 (S)	≤1 (S)	≤1 (S)	≤0.25 (S)	≤0.5 (S)	AmpC positive
	Etest	ND	>256 (R)	1 (S)	>32 (R)	0.094 (S)	0.047 (S)	1.5 (S)	0.25 (S)	1 (S)	0.047 (S)	1.5 (S)	
E. coli (9)	ACC	32 (R)	≤4 (S)	16 (R)	≥8 (R)	0.25 (S)	≤0.25 (S)	≤4 (S)	≤1 (S)	≤1 (S)	≤0.25 (S)	≤0.5 (S)	ESBL positive
	Etest	16 (R)	0.5 (S)	6 (R)	>32 (R)	0.012 (S)	0.016 (S)	0.75 (S)	0.25 (S)	0.5 (S)	0.094 (S)	1 (S)	
E. coli (10)	ACC	≥64 (R)	≤4 (S)	≥32 (R)	≥8 (R)	0.25 (S)	≤0.25 (S)	≤4 (S)	16 (R)	8 (R)	≥8 (R)	2 (S)	ESBL positive
	Etest	64 (R)	0.75 (S)	16 (R)	>32 (R)	0.023 (S)	0.032 (S)	1.5 (S)	0.5 (S)	1 (S)	>32 (R)	1 (S)	
P. aeruginosa (11)	ACC	–	128 (R)	32 (R)	–	–	≥16 (R)	≥128 (R)	≥32 (R)	≥32 (R)	≥8 (R)	≤0.5 (S)	MDR phenotype
	Etest	ND	>256 (R)	96 (R)	ND	ND	>32 (R)	24 (R)	>256 (R)	>256 (R)	>32 (R)	2 (S)	

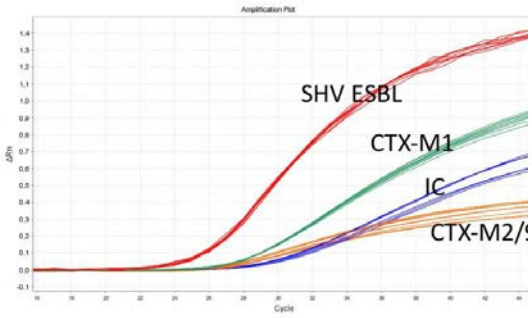
Species ID: 1.35 h – 27.49 hrs before culture-based ID

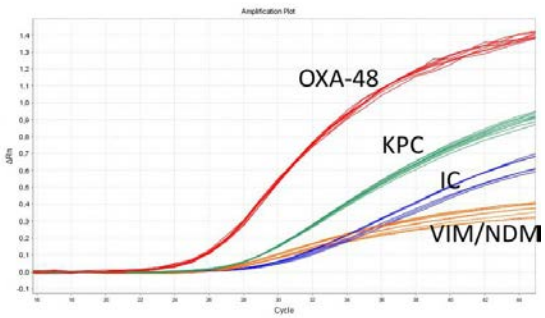
AST: 6.65 h – 40.39 hrs earlier than conventional tests

Check-Direct Screening, Check-Points

Rectal swab
(Copan, ESwab)

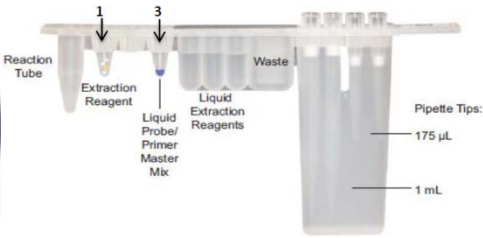
- Rapid preparation
- Time to results (**<3 hrs**)





BD MAX

Reagent strip



Check-Direct ESBL Screen for BD MAX™

CTX-M-1 group
CTX-M-2 group
CTX-M-9 group
SHV-ESBL

Check-Direct CPE Screen for BD MAX™

KPC
OXA-48-like
VIM
NDM

~30 Euro

Performance of the BD MAX™ instrument with Check-Direct CPE real-time PCR for the detection of carbapenemase genes from rectal swabs, in a setting with endemic dissemination of carbapenemase-producing *Enterobacteriaceae* Antonelli *et al.*, DMID, 2016

Florence, Italy
557 rectal swabs

Culture *vs.* C-D direct CPE (2 ≠ master mix)

Limit of detection (LOD)

Target	LOD BDMix (CFU/ml)	LOD CPMix (CFU/ml)
bla_{KPC}	9×10^5	9×10^3
bla_{VIM}	4.5×10^2	4.5×10^2
bla_{OXA-48}	8.5×10^1	8.5×10^1
bla_{NDM}	7.3×10^4	7.3×10^1

ChromID CARBA SMART (w/wo broth enrichment) → [5 samples not detected] *

TAT from 18-24 hrs (direct culture) or 48 hrs (broth enrichment) to 3 hrs

Summary of the results

		Colonization status	
		Positive (n. 29)	*Negative (n. 528)*
CHSM and BERM	*Positive*	24 (82.8 %)[a]	0
	Negative	5 (17.2 %)	528 (100 %)
BDMix	*Positive*	27 (93.1 %)	14 (2.7 %)
	Negative	2 (6.9 %)	496 (93.9 %)
	Unresolved	-	18 (3.4 %)
CPMix	*Positive*	29 (100 %)	15 (2.9 %)
	Negative	0	507 (96.0 %)
	Unresolved	-	6 (1.1 %)

23 KPC
5 VIM
1 OXA-48

Performance of Check-Direct CPE screening for BD MAX

	Positives for bla_{KPC}		Positives for bla_{VIM}		Positives for bla_{OXA-48}		Positives for bla_{NDM}	
	BDMix	CPMix	BDMix	CPMix	BDMix	CPMix	BDMix	CPMix
sensitivity	91,3%	100%	100%	100%	100%	100%	-	-
specificity	98,6%	99,6%	99,3%	97,6%	99,3%	99,6%	100%	100%
PLR	65.21	250	142.86	41.67	-[a]	-	-	-
NLR	0.09	0	0	0	-	-	-	-

Cepheid GeneXpert

- Add aliquot to elution, vortex, transfer to port S
- Insert cartridge to station (overall, **1 min**)
- Run time (**<1 h**)

Real-time multiplex PCR

- Smart fluidic system
- Filtering and Sonication (DNA)
- Fluorescent-labeled hybr. probes (6 colors)
- Internal control

Xpert® Carba-R

KPC
NDM
OXA-48-like
VIM
IMP-1

Xpert® vanA

Xpert® MRSA/SA BC

~50 Euro

MSSA
MRSA
CoNS

Targets: spa, mecA and junction SCCmec-orfX

Multisite Evaluation of Cepheid Xpert Carba-R Assay for Detection of Carbapenemase-Producing Organisms in Rectal Swabs

JCM, 54:7; 2016

M. Tato,[a] P. Ruiz-Garbajosa,[a] M. Traczewski,[b] A. Dodgson,[c] A. McEwan,[c] R. Humphries,[d] J. Hindler,[d] J. Veltman,[e] H. Wang,[f] R. Cantón[a]

4 centers (2 USA, 1 UK, 1 Spain)
July 2013 – Feb 2014

Results obtained in 32-48 min

Xpert Carba-R assay result	Clinical specimens (n = 383)	Contrived specimens (n = 250)	All specimens (n = 633)
Positive (single and/or combined targets)	42	107	149 23.5%
IMP-1	0	25	25
VIM	2	24	26
NDM	2	23	25
KPC	13	19	32
OXA-48	20	15	35
VIM + OXA-48	4	0	4
NDM + KPC	1	0	1
IMP-1 + NDM	0	1	1
Negative	341	143	484

Results by individual targets

Xpert Carba-R assay	Reference method (culture plus sequencing)						
	IMP-1	VIM	NDM	KPC	OXA-48	Negative	Total
IMP-1	26	0	0	0	0	0	26
VIM	0	29	0	0	0	1	30
NDM	0	0	26	0	0	1	27
KPC	0	0	0	29	0	4	33
OXA-48	0	0	0	0	38	1	39
Negative	1	2	0	1	2	3,004	3,010
Total	27	31	26	30	40	3,011	3,165

6 cases of multiple genes (4 not detected by ref. method)
6 out of 154 specimens not detected by Xpert

Performance *vs.* reference method

Xpert Carba-R assay	Reference method (culture plus sequencing)		
	No. positive	No. negative	Total No.
Positive	142	7	149
Negative	6	478	484
Total	148	485	633

Performance for different targets

Target gene	Sensitivity (% [95% CI])	Specificity (% [95% CI])	PPV (%)	NPV (%)
IMP-1	96.3 (81.0–99.9)	100 (99.4–100)	100	99.8
VIM	93.5 (78.6–99.2)	99.8 (99.1–100)	96.7	99.7
NDM	100 (86.8–100)	99.8 (99.1–100)	96.3	100
KPC	96.7 (82.8–99.9)	99.3 (98.3–99.8)	87.9	99.8
OXA-48	95.0 (83.1–99.4)	99.8 (99.1–100)	97.4	99.7

Sensitivity: 96.6% - Specificity: 98.6%

Comparison of the Next-Generation Xpert MRSA/SA BC Assay and the GeneOhm StaphSR Assay to Routine Culture for Identification of *Staphylococcus aureus* and Methicillin-Resistant *S. aureus* in Positive-Blood-Culture Broths

Buchan BW *et al.*, J Clin Microb, 53:3; 2015

Multicenter study (8 hospitals, USA)

795 BCs (30%, *S. aureus*; 13% MRSA)

Identification of *Staphylococcus aureus*

Test	Site	Total no. of specimens tested	No. with result[a]: TP	FP	TN	FN	Sensitivity (% [95% CI])[b]	Specificity (% [95% CI])
Xpert MRSA/SA BC	A	63	19	0	44	0	100 (82.4–100)	100 (92.0–100)
	B	91	32	0	59	0	100 (89.1–100)	100 (93.9–100)
	C	44	17	0	27	0	100 (80.5–100)	100 (87.2–100)
	D	70	26	0	44	0	100 (86.8–100)	100 (92.0–100)
	E	130	27	2[c]	100	1[d]	96.4 (79.7–99.8)	98.0 (92.4–99.6)
	F	211	65	1[e]	145	0	100 (94.5–100)	99.3 (96.2–100)
	G	126	31	0	95	0	100 (88.8–100)	100 (96.2–100)
	H	57	18	0	39	0	100 (81.5–100)	100 (91.0–100)
	Total	792	235	3	553	1	99.6 (97.7–99.9)	99.5 (98.4–99.9)
GeneOhm StaphSR	Total	782	234	19	527	2	99.2 (97.0–99.9)	96.5 (94.6–97.9)

Statistically equivalent

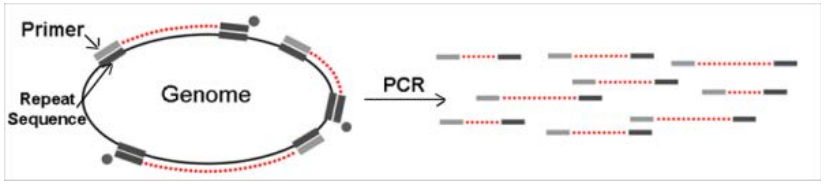
Identification of MRSA

Test	Site	Total no. of specimens tested	No. with result[a]: TP	FP	TN	FN	Sensitivity (% [95% CI])[b]	Specificity (% [95% CI])
Xpert MRSA/SA BC	A	63	11	0	52	0	100 (71.5–100)	100 (93.2–100)
	B	91	16	0	75	0	100 (79.4–100)	100 (95.2–100)
	C	44	7	0	36	1	87.5 (47.3–99.7)	100 (90.3–100)
	D	70	11	1[c]	58	0	100 (71.5–100)	98.3 (90.9–100)
	E	130	10	1[d]	119	0	100 (69.2–100)	99.2 (95.4–100)
	F	211	25	1[c]	185	0	100 (86.3–100)	99.5 (97.0–100)
	G	126	19	0	106	1	95.0 (73.0–99.7)	100 (96.2–100)
	H	57	4	0	53	0	100 (81.5–100)	100 (91.6–100)
	Total	792	103	3	684	2[e]	98.1 (93.3–99.8)	99.6 (98.7–99.9)
GeneOhm StaphSR	Total	782	99	15	662	6[i]	94.3 (88.0–97.9)	97.8 (96.4–98.8)

Statistically equivalent

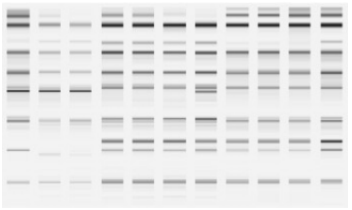
DiversiLab System: rep-PCR

6 hrs

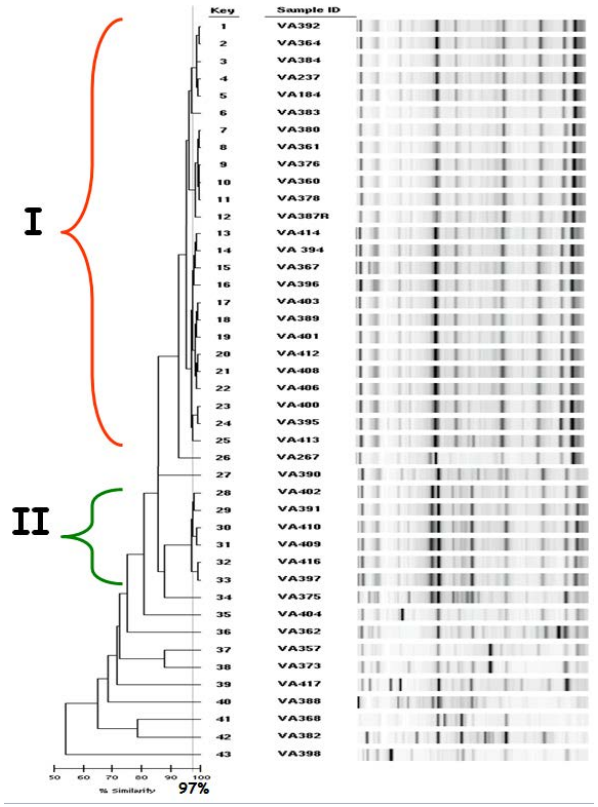


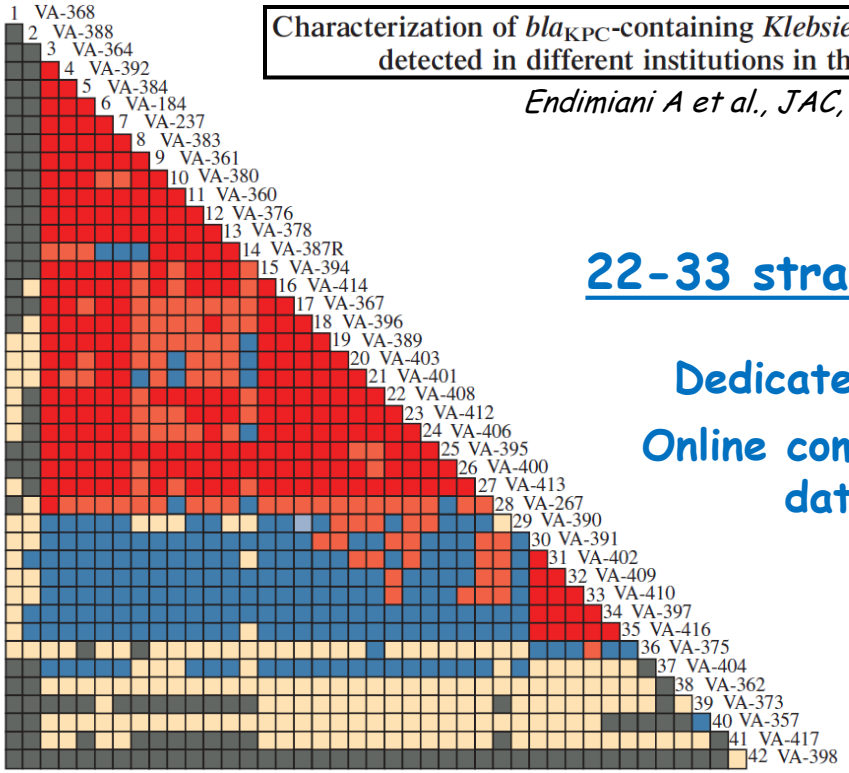
Repetitive extragenic palindromic PCR

1 h



~100 Euro





Characterization of *bla*$_{KPC}$-containing *Klebsiella pneumoniae* isolates detected in different institutions in the Eastern USA

Endimiani A et al., JAC, 2009

22-33 strains in one day

Dedicated software

Online comparison with database

Evaluation of the DiversiLab System for Detection of Hospital Outbreaks of Infections by Different Bacterial Species▽

A. C. Fluit,[1]* A. M. Terlingen,[1] L. Andriessen,[1] R. Ikawaty,[1] R. van Mansfeld,[1] J. Top,[1] J. W. Cohen Stuart,[1] M. A. Leverstein-van Hall,[1,2] and C. H. E. Boel[1]

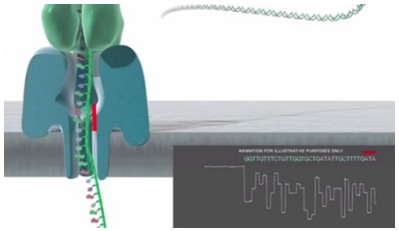
JOURNAL OF CLINICAL MICROBIOLOGY, Nov. 2010,

TABLE 1. Characteristics of DL compared with those of the reference test method

	Species (no. of isolates) and test method	Typeability (%)	Simpson's index of diversity (95% CI)[a]	Adjusted Rand's coefficient	Wallace's coefficient 1	Wallace's coefficient 2
OK	*E. cloacae* (28)					
	DL	100	0.794 (0.632–0.955)	0.691	0.682	0.818
	PFGE	96.4	0.843 (0.703–0.983)			
OK	*Klebsiella* spp. (23)					
	DL	100	0.964 (0.868–0991)	0.623	0.808	1.0
	PFGE	95.7	0.938 (0.894–0.982)			
*Not good**	*E. coli* (38)					
	DL	100	0.972 (0.952–0.992)	0.390	0.450	0.375
	MLVA	100	0.966 (0.941–0.990)			
Not good	*P. aeruginosa* (13)					
	DL	100	0.962 (0.919–1.0)	0.488	1.0	0.333
	PFGE	92.3	0.985 (0.949–1.0)			
	P. aeruginosa (52)					
	DL	100	0.977 (0.958–997)	0.212	0.182	0.333
	MLST	100	0.928 (0.828–0.989)			
OK	*Acinetobacter* spp. (26)					
	DL	100	0.982 (0.966–0.997)	0.908	0.833	1.0
	PFGE	100	0.985 (0.970–0.999)			
OK	*Stenotrophomonas* spp. (25)					
	DL	100	0.963 (0.913–1.0)	0.697	0.6	0.857
	PFGE	96	0.975 (0.937–1.0)			
Not good	*E. faecium* (26)					
	DL	100	0.929 (0.868–0.991)	0.623	0.826	0.543
	MLVA/esp	100	0.892 (0.822–0.962)			
Not good	MRSA (50)					
	DL	100	0.913 (0.859–0.968)	0.266	0.189	0.571
	Hospital hygiene classification	100	0.976 (0.960–0.991)			
	MRSA (50)					
	DL	100	0.913 (0.859–0.968)	0.261	0.198	0.568
	PFGE	100	0.970 (0.953–0986)			
	MRSA (50)					
	DL	100	0.913 (0.859–0.968)	0.303	0.377	0.354
	spa typing	100	0.908 (0.858–0.957)			
	MRSA (50)					
	DL	100	0.913 (0.859–0.968)	0.252	0.189	0.571
	MLVA	100	0.971 (0.955–0.988)			

Oxford Nanopore Sequencing

~500 Euro



~200-300 Euro

Rapid real-time long read WGS (Point of care, POC)

Emergence of *Klebsiella pneumoniae* co-producing NDM-1, OXA-48, CTX-M-15, CMY-16, QnrA and ArmA in Switzerland

IJAA, 2014

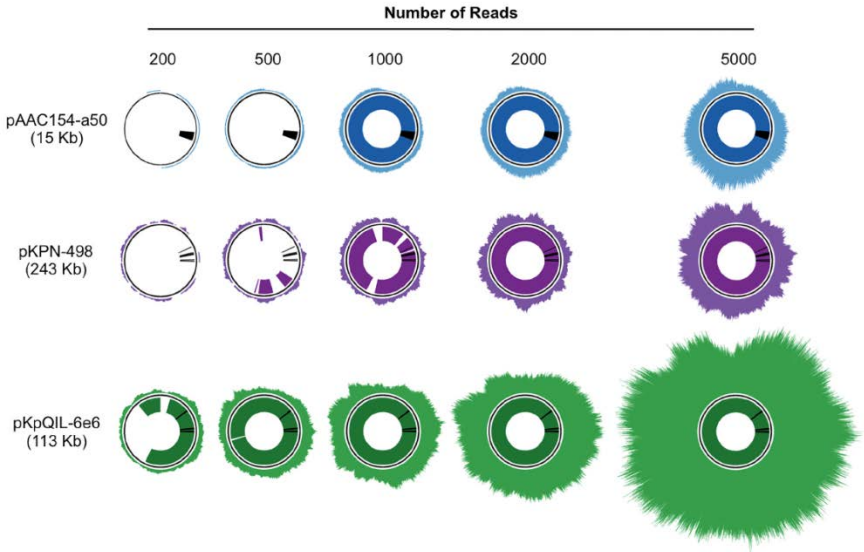
Salome N. Seiffert[a,b,c], Jonas Marschall[d], Vincent Perreten[b], Alessandra Carattoli[a,b,e], Hansjakob Furrer[d], Andrea Endimiani[a,*]

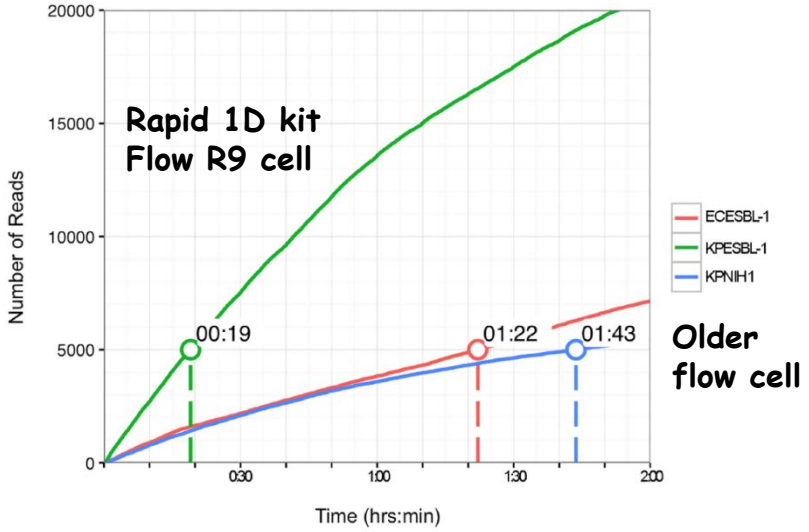
Our experience: ~3 hrs for WGS

Rapid Nanopore Sequencing of Plasmids and Resistance Gene Detection in Clinical Isolates

J. Clin. Microbiol. 11 October 2017

Jamie K. Lemon, Pavel P. Khil, Karen M. Frank, and John P. Dekker[#]





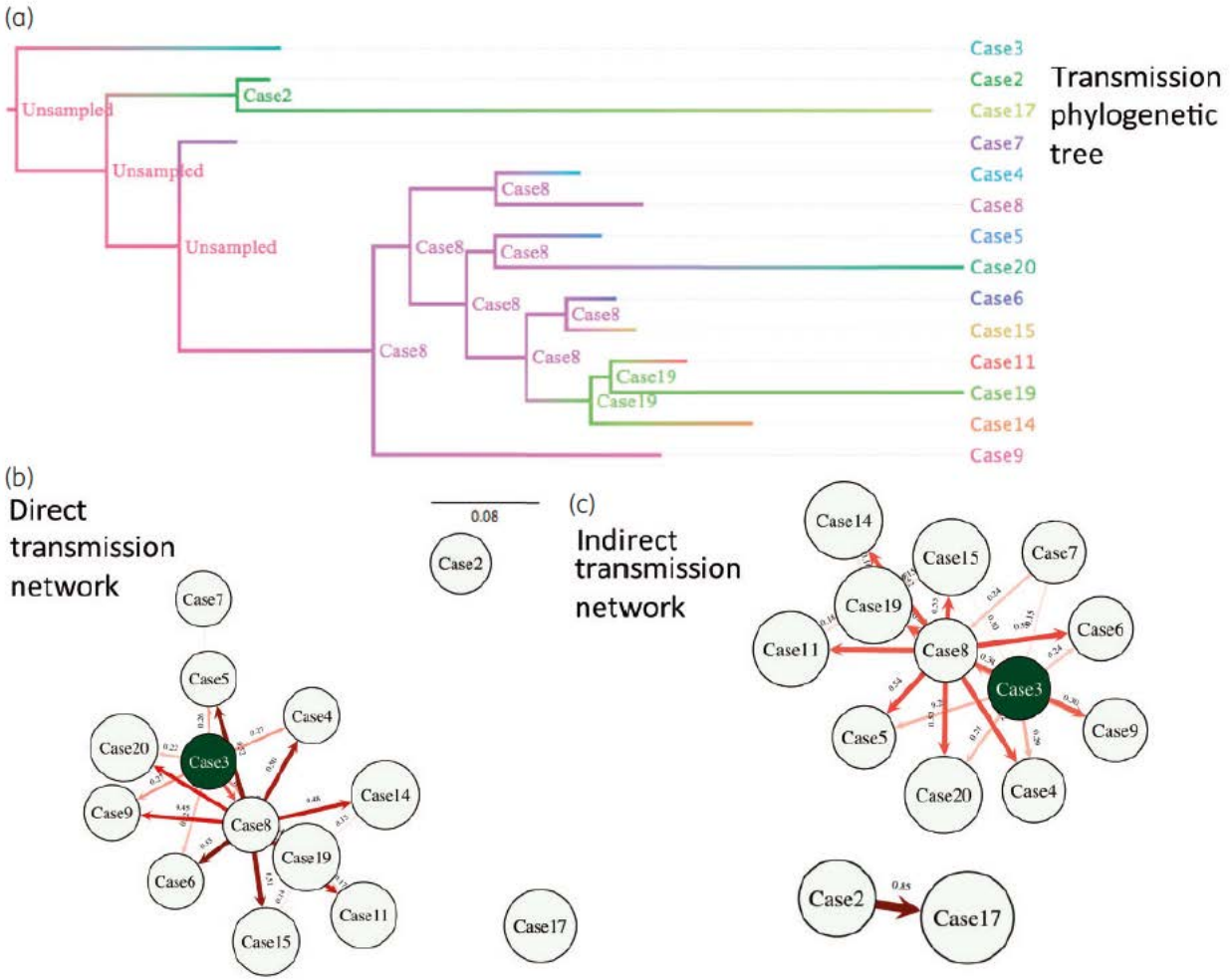
Covert dissemination of carbapenemase-producing *Klebsiella pneumoniae* (KPC) in a successfully controlled outbreak: long- and short-read whole-genome sequencing demonstrate multiple genetic modes of transmission

J Antimicrob Chemother 2017; **72**: 3025–3034

UK, 2013-14

Rectal swabs/clinical samples

MinION and Illumina

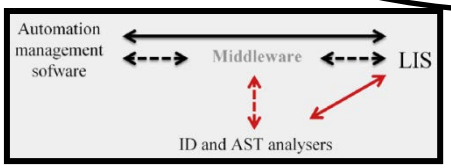


Clonal?

Plasmid?

Tn4401?

"Integrated automation"



Rapid, accurate, cost-effective, information for treating physicians

BETTER OUTCOME

Disadvantages

No laboratory adaptation to automation (e.g. staff shifts, training, 24/7)

- Misuse of tools
- Expectations for increased productivity not achieved

Crash of automat (backup needed).

- Good support and maintenance essential.
- Expensive maintenance budget.

Staff turnover (boring and lonely work?).

- Lab automation needs to be a project that includes everybody.
- Aim is not to replace experienced laboratory technicians but to assist them in their daily tasks.

Only eye is used.

- Smelling or other sensing of colony consistency disappears.
- More difficult to identify unusual/new species.

Security.

- Inoculation of sensitive samples (e.g. sputum, blood culture).
- Contamination of specimen processors and incubators (e.g. fungus spores, biosafety class 3 microorganisms).

Loss of microbiologic knowledge.

- Decrease in analytical variability.
- Standardized microbiologic factory (you find what you are looking for).

Clinical Microbiology and Infection, Volume 22 Number 3, March 2016

to new insights into disease pathogenesis. It is true that we will need a considerable amount of expertise to work with these advanced approaches. However, it is also imperative for us to accept these challenges and to enact wise choices in the selection of diagnostics. We are not certain which method will best suit our needs, but, perhaps, "*chance will favor a prepared mind*".

Robert A. Bonomo and Andrea Endimiani, DMID, 2013

THANK YOU!

Institute for Infectious Diseases - University of Bern, Switzerland

- Odette J. Bernasconi (PhD student)*
- Fernanda Pimentel (PhD student)
- Thomas Büdel (Lab Technician)
- Dr. med. Baharak Babouee-Flury (PostDoc)

FNSNF
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